MAP Pharmaceuticals, Inc.
Form 10-K
March 05, 2010
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2009

OR

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from _____ to _____

Commission File Number 001-33719

MAP PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**20-0507047**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

2400 Bayshore Parkway, Suite 200

Mountain View, California	**94043**
(Address of principal executive offices)	**(Zip code)**

(650) 386-3100

(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock per share $0.01 par value	**The NASDAQ Global Market**

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ¨ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of large accelerated filer, accelerated filer, and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer x
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined by Rule 12b-2 of the Exchange Act). Yes ¨ No x

The aggregate market value of the voting and non-voting common equity stock held by non-affiliates of the registrant was $113,032,495 as of June 30, 2009, the last day of the registrant s second fiscal quarter during its fiscal year ended December 31, 2009, based upon the closing sale

price on The NASDAQ Global Market reported for such date. Shares of Common Stock held by each officer and director and by each person who may be deemed to be an affiliate have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 28, 2010, the registrant had outstanding 26,302,226 shares of Common Stock.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s proxy statement to be filed with the Securities and Exchange Commission, or the SEC, pursuant to Regulation 14A in connection with the registrant s 2010 Annual Meeting of Stockholders, to be filed subsequent to the date hereof, are incorporated by reference into Part III of this Annual Report on Form 10-K. Such proxy statement will be filed with the SEC not later than 120 days after the conclusion of the registrant s fiscal year ended December 31, 2009.

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PART I

ITEM 1. BUSINESS

Overview

Our goal is to use our proprietary inhalation technologies to enhance the therapeutic benefits and commercial attractiveness of proven drugs while minimizing risk by capitalizing on their known safety, efficacy and commercialization history. We have proprietary product candidates in development that address large market opportunities. Our current focus is to advance our Phase 3 product candidate, LEVADEX orally inhaled migraine therapy, formerly known as MAP0004, a proprietary orally inhaled version of dihydroergotamine mesylate, or DHE, for the potential treatment of migraine.

LEVADEX

Migraine is a chronic and debilitating neurological disorder characterized by episodic attacks. Migraine attacks typically manifest themselves as moderate to severe headache pain, with associated symptoms that often include nausea and vomiting, photophobia, phonophobia, and visual disturbances or aura. They usually involve pounding or throbbing pain on one side of the head, although pain may occur on both sides. Migraines limit the normal functioning of patients, who often seek dark, quiet surroundings until the episode has passed. Most migraines last between four and 24 hours, but some last as long as three days. According to published studies, the median frequency of attack is 1.5 times per month, although approximately 25% of migraine sufferers experience one or more attacks every week.

Migraine is a major public health problem that affects up to approximately 12% of the population in the United States and approximately 15% in Europe. According to the National Headache Foundation, approximately 30 million people in the United States suffer from migraine. In 2008, according to market data, approximately 29 million prescriptions were written for the treatment of migraine in the United States. Approximately 12 million of those prescriptions were written for acute migraine specific drugs. The majority of acute migraine specific drug prescriptions written were in the triptan class. In 2009, the triptan market in the United States totaled approximately $2.1 billion in revenues.

We have designed LEVADEX to provide faster onset and longer-lasting migraine relief than triptans, the class of drugs most often prescribed for treating migraine. LEVADEX is an easy to use, at-home therapy in development that patients self-administer using our proprietary hand-held Tempo® inhaler. DHE currently is available as an intravenous, or IV, therapy which has been used in clinical settings for over 50 years for the safe and effective treatment of migraine, particularly forms of migraine that are severe or do not respond to triptans or other therapies. DHE also is available in an intranasal formulation. We believe LEVADEX has the potential to be suitable as a first-line therapy for some migraine patients.

In May 2009, we announced results of the efficacy portion of our first Phase 3 clinical trial of LEVADEX, or FREEDOM-301, which is being conducted pursuant to a special protocol assessment, or SPA, from the U.S. Food and Drug Administration, or FDA. We announced that the clinical trial met its four primary endpoints, pain relief and being nausea, phonophobia and photophobia free as reported two hours after dosing. Additional endpoints showed that LEVADEX provided rapid and sustained pain relief for up to 48 hours after dosing.

Patients taking LEVADEX therapy had statistically significant improvement at two hours compared to patients on placebo for each of the primary endpoints:

Pain relief: 58.7 percent of patients who received LEVADEX compared with 34.5 percent for placebo ($p<0.0001$);

Phonophobia free: 52.9 percent of patients who received LEVADEX compared with 33.8 percent for placebo ($p<0.0001$);

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Photophobia free: 46.6 percent of patients who received LEVADE compared with 27.2 percent for placebo (p<0.0001); and

Nausea free: 67.1 percent of patients who received LEVADEX compared with 58.7 percent for placebo (p=0.02).

A total of 792 patients were included in the primary data analysis as specified in the protocol of the FREEDOM-301 study. The patient population studied had more severe migraine pain than anticipated, with 46 percent reporting severe pain and 54 percent reporting moderate pain prior to administration of the study drug.

Results from additional pre-defined analyses include:

LEVADEX therapy achieved statistically significant onset of pain relief at 30 minutes after dosing (p=0.03);

While not statistically significant, 50% more of the patients receiving LEVADEX therapy than the patients receiving placebo reported pain relief at 10 minutes;

LEVADEX therapy achieved statistically significant sustained pain relief from two to 24 hours (p<0.0001), as well as two to 48 hours (p<0.0001, when unadjusted for multiplicity);

LEVADEX therapy achieved statistically significant pain freedom (pain symptom score = 0) as early as 30 minutes (p=0.002, when unadjusted for multiplicity); and

LEVADEX therapy achieved sustained pain freedom from two to 24 hours, as well as two to 48 hours (p<0.0001 for both time points, when unadjusted for multiplicity).

LEVADEX was well tolerated, with the most common adverse event reported being medication aftertaste at six percent, with two percent of patients receiving placebo also reporting medication aftertaste. The next most common adverse event was nausea at five percent, compared with two percent for placebo. Symptoms or sensitivities typically associated with commonly used triptan migraine treatments, such as chest discomfort (one percent) or chest pain (0 percent), were rare and comparable to placebo. There were no mean decreases in lung function, as measured by spirometry, between the active and placebo groups. There were no drug-related serious adverse events reported in the trial. These data were presented in September 2009 in a late-breaking session of the 14th Congress of the International Headache Society.

In September 2009, we announced that post-hoc analysis of data from this Phase 3 trial shows the potential of LEVADEX to be effective in treating acute migraine as well as a broad spectrum of migraine, including migraine subpopulations that are often resistant to current therapies such as triptans, migraine with moderate and severe pain, migraine with nausea and vomiting and migraine with and without aura.

In October 2009, we announced that we had completed a planned interim safety review of the open-label, long-term safety extension of the FREEDOM 301 clinical trial. At the time of the interim review, more than 400 patients had completed at least six months of treatment and over 7,800 headaches had been treated in the safety extension. No drug-related serious adverse events had been reported.

In January 2010, we announced that the FDA had informed us that a second pivotal efficacy study would not be required for the LEVADEX new drug application, NDA, submission. We had previously anticipated initiating a second pivotal efficacy study in the first quarter of 2010.

The remaining clinical studies for the LEVADEX program include the ongoing 12 month open-label safety extension of the FREEDOM-301 clinical trial, a pharmacokinetics, PK, trial and a pharmacodynamics, PD, trial. We anticipate that patients and subjects in these studies will complete treatment in 2010.

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We hold worldwide commercialization rights for LEVADEX and our goal is to market LEVADEX in the United States through our own focused sales force targeting neurologists and headache specialists. We may establish partnerships with pharmaceutical companies to market and sell to primary care physicians and specialists inside and outside of the United States.

Nebulized Budesonide

Unit Dose Budesonide, or UDB, is our proprietary nebulized version of budesonide intended to treat asthma in children from 12 months to eight years of age. UDB is designed to be administered more quickly and to provide efficacy at lower doses than conventional nebulized budesonide. Conventional nebulized budesonide is an inhaled corticosteroid approved by the FDA, for treating asthma in children from 12 months up to eight years of age. Our UDB product candidate has been designed to achieve a particle size smaller than previously possible with budesonide. We believe this smaller particle size may allow for faster delivery and efficacy at a lower dose, which together may offer improved safety, compliance and convenience.

In December 2008 we entered into a worldwide collaboration with AstraZeneca AB to develop and commercialize UDB, which became effective on February 2, 2009. In February 2009, we announced top-line results from our first Phase 3 trial of UDB, indicating that the trial did not meet its co-primary endpoints when compared to placebo. On July 8, 2009, we received a notice of termination of the collaboration agreement from AstraZeneca. Subsequently, we suspended development of UDB. We are considering options for our pediatric asthma program moving forward, by leveraging our experience with budesonide and our expertise in particle technology, including the development of a next generation therapy with budesonide.

Other Pipeline Products

Our product portfolio also includes the two earlier stage product candidates listed below, both of which highlight the broad applicability of our technologies to a diverse range of potential future products. While we do not plan to make further significant direct investment in these two product candidates, we plan to evaluate other potential product candidates which may utilize these technologies, as well as potential partnership opportunities for further development and commercialization of these two product candidates.

Combination Particle Technology: We are applying our proprietary particle formulation technologies to deliver the optimal ratio of multiple drugs in a reproducible and consistent manner. We combine two or more drugs together into a single micron sized particle at consistent and reproducible ratios, which may improve the delivery profile and stability of the resultant combination therapy. We believe our proprietary technologies in this area have potential broad applicability for a number of small molecule combination product candidates in diverse indications via inhalation and other routes of delivery.

MAP0005: We are demonstrating this combination particle capability with MAP0005, our proprietary single particle combination of an inhaled corticosteroid and a long-acting beta-agonist, or LABA, for the potential treatment of asthma and chronic obstructive pulmonary disease, or COPD, using our proprietary Tempo inhaler. In April 2008, we announced positive results from a Phase 2a clinical trial evaluating MAP0005 in adult asthmatics.

Stable Protein & Peptide Technology: We have also demonstrated our ability to apply our proprietary technologies to formulate and stabilize biologically-active proteins and peptides. We design and incorporate our protein formulations without the need for excipients or other additives, to be stored for months at room temperature and to provide multiple doses of medicine delivered accurately without the need for needle injections.

MAP0001: We are demonstrating this stable protein and peptide capability with MAP0001, our proprietary formulation of insulin for the potential treatment of Type 1 and Type 2 diabetes via pulmonary delivery using our proprietary Tempo inhaler. This approach may overcome many of the issues currently associated with the invasive delivery of proteins by injection or infusion in general, and with inhalable insulin therapies in particular.

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We have not filed an investigational new drug application, or IND, with the FDA for MAP0005 or MAP0001 because our clinical trials were not conducted in the United States.

A core part of our strategy is to reduce the risk of drug development by focusing on the development of proven drugs with established safety and efficacy profiles. The compounds underlying our product candidates are well characterized and have been previously approved by the FDA for other sponsors and in other dosage forms and formulations. As a result, we may seek FDA marketing approval of our product candidates under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FFDCA, which, if available to us, would allow any NDA we file with the FDA to rely in part on data in the public domain or the FDA s prior conclusions regarding the safety and effectiveness of approved compounds. This may expedite the development program for our product candidates by potentially decreasing the overall scope of work we must do ourselves.

Our Product Candidates

LEVADEX for the Acute Treatment of Migraine

LEVADEX, or MAP0004, is our proprietary orally inhaled version of DHE in development intended to treat migraine. In a Phase 3 clinical trial, LEVADEX provided pain relief at 10 minutes after dosing for some patients, and provided statistically significant pain relief at 30 minutes and two hours after dosing. In addition, LEVADEX provided sustained pain relief from two to 24 hours and two to 48 hours. LEVADEX was well tolerated and there were no drug-related serious adverse events reported. Symptoms and sensitivities typically associated with triptans were rare and similar to placebo. Additional analyses indicated the potential of LEVADEX to effectively treat any time during the migraine including four to eight hours after onset of migraine. Based on these results, we believe LEVADEX has the potential to be suitable as a first-line therapy for some migraine patients. Migraine is a syndrome characterized by four symptoms: pain, nausea, phonophobia, or abnormal sensitivity to sound, and photophobia, or abnormal sensitivity to light. LEVADEX is an easy to use, non-invasive, at-home therapy in development that patients self-administer using our proprietary hand-held Tempo inhaler. DHE is available as an IV therapy which has been used in clinical settings for over 50 years for the safe and effective treatment of migraine, particularly forms of migraine that are severe or do not respond to triptans or other therapies. We believe DHE s adoption as a first-line therapy has been limited by its invasive mode of administration and high incidence of nausea. In May 2009, we announced results of the efficacy portion of our first Phase 3 clinical trial of LEVADEX, or FREEDOM-301, which is being conducted pursuant to a SPA, from the FDA. We announced that the clinical trial met its four primary endpoints, pain relief and being nausea, phonophobia and photophobia free as reported two hours after dosing. Additional endpoints showed that LEVADEX provided rapid and sustained pain relief for up to 48 hours after dosing. In January 2010, we announced that the FDA had informed us that a second pivotal efficacy study would not be required for the LEVADEX NDA submission. We had previously anticipated initiating a second pivotal efficacy study in the first quarter of 2010.

Migraine

Migraine is a chronic and debilitating neurological disorder characterized by episodic attacks. Migraine attacks typically manifest themselves as moderate to severe headache pain, with associated symptoms that often include nausea and vomiting, photophobia, phonophobia, and visual disturbances or aura. They usually involve pounding or throbbing pain on one side of the head, although pain may occur on both sides. Migraines limit the normal functioning of patients, who often seek dark, quiet surroundings until the episode has passed. Most migraines last between four and 24 hours, but some last as long as three days. According to published studies, the median frequency of attack is 1.5 times per month, although approximately 25% of migraine sufferers experience one or more attacks every week.

Migraine is a major public health problem that affects up to approximately 12% of the population in the United States and approximately 15% in Europe. According to the National Headache Foundation, approximately 30 million people in the United States suffer from migraine. In 2008, according to market data, approximately 29 million prescriptions were written for the treatment of migraine in the United States. Approximately 12 million of those prescriptions were written for acute migraine specific drugs. The majority of acute migraine

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specific drug prescriptions written were in the triptan class. In 2009, the triptan market in the United States totaled approximately $2.1 billion in revenues. There are two general categories of migraine therapies: acute and preventive. Acute therapies dominate the migraine market and are used during infrequent attacks, typically characterized as one to three attacks per month, and are designed to relieve the pain, nausea, phonophobia and photophobia symptoms of migraine. The goals of acute therapy are to stop the attack quickly and consistently, while preventing recurrence, to maintain the patient s ability to function, to use the least amount of medication and to limit adverse side effects. Although triptans are the predominant class of drugs used to specifically target migraine, DHE is another class of acute, migraine-specific therapy.

Limitations of Current Migraine Therapies

The type of migraine treatment pursued depends on the frequency and severity of the headache, speed of onset and previous response to medication. In published studies, migraine sufferers often cite faster onset of pain relief and lower incidence of migraine recurrence as two key therapeutic attributes they would like from their medication. Treatment typically involves patients self-medicating with over-the-counter drugs when pain is mild and attacks are infrequent. Patients with more frequent or severe migraine or those who do not respond to simple analgesics may seek medical attention with a primary care physician initially and then with a headache clinic or neurology specialist, if needed. Once a physician has diagnosed migraine, triptans are generally prescribed. If a patient does not respond to one triptan, the physician may switch to another, as the response to various triptans is unpredictable.

Triptans have three major limitations:

Slow and variable onset: While triptans have improved the treatment of migraine, the onset of pain relief with these products tend to be relatively slow and variable due to inconsistent systemic absorption via oral and nasal routes of administration.

Not broadly efficacious: Approximately 30% to 40% of migraine patients do not fully respond to the first triptan prescribed. Migraine patients who do not respond to any triptan therapy have few satisfactory alternatives.

Side effects: Triptans may constrict arteries, which may raise blood pressure.

DHE is an acute therapy and alternative to triptans that has been used for more than 50 years to safely treat migraine. Many headache specialists consider DHE to be the standard of care in treatment of status migrainosus, which is a condition characterized by debilitating migraines that last more than 72 hours. Although DHE overcomes many of the limitations of triptans, historically it also has had its own limitations, including the following:

Inconvenient and inconsistent dosing: DHE has been available predominantly for administration nasally and intravenously. Intravenous administration of DHE requires the supervision of a healthcare provider and is typically performed in a headache clinic or hospital setting, which is expensive and requires the patient to travel to one of these locations while suffering with the migraine. Absorption of DHE via the nasal pathway may lead to inconsistent dosing, and generally takes 30 to 60 minutes to provide significant pain relief. Nasal administration of DHE may result in unpleasant taste, and can cause congestion or irritation of the nasal membrane.

Side effects: One of the common side effects of conventional DHE administered intravenously is nausea. Patients who receive DHE intravenously are often given an anti-nausea medication at the same time.

Our Potential Solution: LEVADEX

Based on our Phase 3 clinical trial, we believe that LEVADEX may provide patients with the following benefits when compared to existing migraine therapies:

Rapid onset: The inhalation of DHE via our Tempo inhaler offered fast onset of pain relief. In our Phase 3 clinical trial, LEVADEX provided significant pain relief at 30 minutes after dosing. In addition, while not statistically significant, 50% more of the patients receiving LEVADEX than the patients receiving placebo reported pain relief at 10 minutes.

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Long-lasting: In our Phase 3 clinical trial, LEVADEX provided long-lasting pain relief with low incidence of recurrence, and provided sustained pain relief through 48 hours.

Efficacy at any time after the start of migraine: Additional analyses indicated the potential of LEVADEX to effectively treat at any time during the migraine including within one hour, and after eight hours from the start of migraine.

Broadly efficacious: Based on historical DHE use, LEVADEX may provide a higher response rate and has the potential to treat patients who have not previously responded to other therapies, such as triptans. We also believe that LEVADEX has the potential to treat a broad spectrum of migraine, including migraine subpopulations that are often difficult to treat, such as menstrual migraine, morning migraine, migraine with allodynia, migraine associated with severe pain and migraine with nausea and vomiting.

Low incidence of side effects: In our Phase 3 clinical trial, LEVADEX was well tolerated, with the most common adverse event reported being medication aftertaste at six percent, with two percent of patients receiving placebo also reporting medication aftertaste. The next most common adverse event was nausea at five percent, compared with two percent for placebo. Symptoms or sensitivities typically associated with commonly used triptan migraine treatments, such as chest discomfort or chest pain, were rare and comparable to placebo.

Convenient and consistent delivery: LEVADEX is non-injectable and designed to be easy to use, which may result in increased patient comfort and compliance. The clinical trial was performed in the home, without clinical supervision and with minimal training. In a previous trial, dose-to-dose variability was comparable to solid oral dosage forms.

LEVADEX Clinical Development Program

In May 2009, we announced results of the efficacy portion of our first Phase 3 clinical trial of LEVADEX, or FREEDOM-301, which is being conducted pursuant to an SPA from the FDA. We announced that the clinical trial met its four primary endpoints, pain relief and being nausea, phonophobia and photophobia free as reported two hours after dosing. Additional endpoints showed that LEVADEX provided rapid and sustained pain relief for up to 48 hours after dosing.

Phase 3 Clinical Trial Results. We evaluated the safety and efficacy of LEVADEX as a potential acute treatment for migraine in a Phase 3 multi-center, randomized, double-blind, placebo-controlled trial followed by a 12-month open-label safety assessment. In this trial, patients were randomized to either 0.5 mg LEVADEX or placebo during the efficacy portion of the trial. This clinical trial is being conducted pursuant to an SPA with the FDA.

In May 2009, we announced results of the efficacy portion of our first Phase 3 clinical trial of LEVADEX, or FREEDOM-301. We announced that the clinical trial met its four primary endpoints, pain relief and being nausea, phonophobia and photophobia free as reported two hours after dosing. Additional endpoints showed that LEVADEX provided rapid and sustained pain relief for up to 48 hours after dosing.

Patients taking LEVADEX therapy had statistically significant improvement at two hours compared to patients on placebo for each of the primary endpoints:

Pain relief: 58.7 percent of patients who received LEVADEX compared with 34.5 percent for placebo ($p<0.0001$);

Phonophobia free: 52.9 percent of patients who received LEVADEX compared with 33.8 percent for placebo ($p<0.0001$);

Photophobia free: 46.6 percent of patients who received LEVADE compared with 27.2 percent for placebo ($p<0.0001$); and

Nausea free: 67.1 percent of patients who received LEVADEX compared with 58.7 percent for placebo (p=0.02).

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A total of 792 patients were included in the primary data analysis as specified in the protocol of the FREEDOM-301 study. The patient population studied had more severe migraine pain than expected, with 46 percent reporting severe pain and 54 percent reporting moderate pain prior to administration of the study drug.

Results from additional pre-defined analyses include:

- LEVADEX therapy achieved statistically significant onset of pain relief at 30 minutes after dosing (p=0.03);
- While not statistically significant, 50% more of the patients receiving LEVADEX therapy than the patients receiving placebo reported pain relief at 10 minutes;
- LEVADEX therapy achieved statistically significant sustained pain relief from two to 24 hours (p<0.0001), as well as two to 48 hours (p<0.0001, when unadjusted for multiplicity);
- LEVADEX therapy achieved statistically significant pain freedom (pain symptom score = 0) as early as 30 minutes (p=0.002, when unadjusted for multiplicity); and
- LEVADEX therapy achieved sustained pain freedom from two to 24 hours, as well as two to 48 hours (p<0.0001 for both time points, when unadjusted for multiplicity).

LEVADEX was well tolerated, with the most common adverse event reported being medication aftertaste at six percent, with two percent of patients receiving placebo also reporting medication aftertaste. The next most common adverse event was nausea at five percent, compared with two percent for placebo. Symptoms or sensitivities typically associated with commonly used triptan migraine treatments, such as chest discomfort (one percent) or chest pain (0 percent), were rare and comparable to placebo. There were no decreases in lung function, as measured by spirometry, between the active and placebo groups. There were no drug-related serious adverse events reported in the trial. These data were presented in September 2009 in a late-breaking session of the 14th Congress of the International Headache Society.

In September 2009, we announced that post-hoc analysis of data from this Phase 3 trial shows the potential of LEVADEX to be effective in treating acute migraine as well as a broad spectrum of migraine, including migraine subpopulations that are often resistant to current therapies such as triptans, migraine with moderate and severe pain, migraine with nausea and vomiting and migraine with and without aura.

In October 2009, we announced that we had completed a planned interim safety review of the open-label, long-term safety extension of the FREEDOM 301 clinical trial. At that point, more than 400 patients had completed at least six months of treatment and over 7,800 headaches had been treated in the safety extension. No drug-related serious adverse events had been reported. The goal of the ongoing long-term safety extension is to evaluate overall safety, including pulmonary and cardiovascular safety, of LEVADEX in at least 300 patients for six months and in at least 150 patients, including migraine sufferers with asthma, for 12 months as part of a potential NDA. The interim review of the data was conducted after a pre-specified number of patients had completed six months of exposure to LEVADEX and was also reviewed by an independent Data Monitoring Committee, DMC. The DMC is an independent group of clinical trial experts, including physicians, formed to critically review and evaluate patient safety data generated in the FREEDOM 301 trial with the objective of ensuring clinical trial patient safety, quality of the data collected and continued scientific validity of the trial design. On an ongoing basis, the DMC reviews data from the safety extension, including results of both pulmonary lung function evaluations using measures such as DLco and FEV_1 and cardiac evaluations using electrocardiograms, echocardiograms and chest X-rays.

In January 2010, we announced that the FDA had informed us that a second pivotal efficacy study would not be required for the LEVADEX NDA submission. We had previously anticipated initiating a second pivotal efficacy study in the first quarter of 2010.

The remaining clinical studies for the LEVADEX program include the ongoing 12 month open-label safety extension of the FREEDOM-301 study, a PK study and a PD study. The PK study will compare the safety, PK

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and metabolic profiles of LEVADEX with IV DHE in smokers and non-smokers. The PD study will evaluate pulmonary artery pressure in healthy volunteers using echocardiograms. We anticipate that patients and subjects in these studies will complete treatment in 2010.

Phase 2 Clinical Trial Results. In March 2007, we announced positive results from two Phase 2 clinical trials with LEVADEX for the acute treatment for migraine.

The objective of the first Phase 2 clinical trial was to evaluate the efficacy and tolerability of three different doses of LEVADEX in adult migraine patients when self-administered at home. This Phase 2 clinical trial was a randomized, double blind, placebo-controlled trial of three doses of LEVADEX in 86 patients. The clinical trial consisted of two treatment periods. The first treatment period evaluated two doses of LEVADEX, 1.0 mg and 0.5 mg versus placebo and the second treatment period re-randomized responders in the first treatment period to evaluate a lower dose, 0.25 mg versus placebo. In the first treatment period, the 0.5 mg dose of LEVADEX showed pain relief in 32% of the patients at ten minutes ($p = 0.019$), pain relief in 72% of the patients at two hours, the clinical trial s primary endpoint ($p = 0.019$), and sustained pain relief in 43% of the patients at 24 hours ($p = 0.066$) in a treatment received population. Unlike conventional IV DHE, which is generally administered with an anti-nausea medication, LEVADEX was administered by itself and showed no statistically significant drug related increase in nausea. LEVADEX was also shown in the clinical trial to be well tolerated, with no serious adverse events reported. In the second treatment period, 35 subjects were randomized to treat a second subsequent migraine with a 0.25 mg dose versus placebo. No significant benefit was seen with this lowest dose when compared to placebo.

The objective of the second Phase 2 clinical trial was to evaluate the safety and tolerability of LEVADEX in subjects with asthma and to demonstrate that the blood levels of the drug achieved by the therapy were similar to those seen after inhalation by subjects with healthy lungs. This second Phase 2 clinical trial was a randomized, double blind, placebo-controlled trial in 19 adult asthmatics. Each patient received three doses, one every week in randomized order over a 15-day period, including two 1.0 mg doses of LEVADEX and one dose of placebo. The clinical trial indicated that LEVADEX was well tolerated by subjects with compromised lung function, and that the pharmacokinetics of LEVADEX, or distribution of the drug in the body, was similar to that experienced by adults with healthy lungs as shown in an earlier Phase 1 clinical trial. No serious or significant drug related adverse events were reported. In addition, no clinically significant changes were observed in pulmonary function tests, heart rate, blood pressure, respiratory rate or mean IgE levels, a measure of systemic immune response, or the body s defenses reacting to a foreign substance.

We believe that, based on our pharmacokinetics and receptor binding research, LEVADEX s administration via the lung may provide an opportunity to retain the efficacy attributes seen with IV DHE while minimizing the potential side effects often seen during IV DHE administration. Pharmacokinetics data suggest that LEVADEX closely mimics the blood levels and the time to maximum drug concentration seen with effective doses of DHE administered intravenously. However, unlike IV administration of DHE, we do not expect LEVADEX to cause significant treatment related nausea which may be a factor that has limited the usage of IV DHE outside the headache clinic or hospital. In our Phase 1 trial comparing IV DHE to LEVADEX, the blood levels of drug were similar. However, the maximum drug concentration for inhaled DHE administered with our Tempo inhaler was approximately 11 to 13 fold lower than that for IV DHE, which we believe in part accounts for the low incidence of drug-induced nausea observed in our clinical trials to date.

In addition, we have conducted pre-clinical animal studies to evaluate lung toxicity and coronary vascular effects of our proprietary formulation of DHE. In our six month chronic inhalation toxicity assessment of DHE, where animals were exposed to up to 1.08 mg/kg (more than 46 times the maximum potential recommended daily dose of LEVADEX, if approved) of DHE per day for six months, there was no significant respiratory tract toxicity observed. In another pre-clinical study designed to evaluate cardiovascular parameters, we observed no significant differences in coronary vascular effects comparing inhaled DHE to IV DHE.

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Because DHE is well characterized and previously approved, we may seek FDA marketing approval of LEVADEX under Section 505(b)(2) of the FFDCA. Section 505(b)(2) of the FFDCA provides an alternate path to FDA approval for modifications to formulations of products previously approved by the FDA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. This may expedite the development program for LEVADEX by potentially decreasing the overall scope of work we must do ourselves.

Other Potential Uses and Indications for LEVADEX

We plan to consider development of LEVADEX for use outside the United States as well as for potential additional indications beyond acute migraine.

We believe there is opportunity to develop LEVADEX for potential use outside of the United States. While acute migraine is a major public health problem affecting approximately 12% of the population in the United States, it also affects approximately 15% of the population in Europe. Based on the accumulated nonclinical and clinical data to date, we believe there may be significant commercial opportunities for LEVADEX outside of the United States.

Furthermore, based on key LEVADEX attributes observed to date, including fast onset of action, long duration of effect as well as historical uses for DHE, developing additional indications for LEVADEX may represent significant opportunities. We believe LEVADEX has the potential to treat additional migraine indications such as cluster headache, menstrual migraine, adolescent migraine, chronic migraine, chronic daily headache and status migrainosus.

Nebulized Budesonide for the Treatment of Asthma in Children

Our proprietary nebulized version of budesonide is for the potential treatment of asthma in children from 12 months to eight years of age. We design our nebulized budesonide to be administered more quickly and to provide efficacy at doses lower than those approved for conventional nebulized budesonide, which is the current leading nebulized treatment for asthma in children. Conventional nebulized budesonide is an inhaled corticosteroid, or ICS, approved by the FDA for treating asthma in children from 18 months up to eight years of age. Conventional nebulized budesonide was first introduced as Pulmicort Respules in Europe in 1990 and in the United States in 2000. We design nebulized budesonide to have a particle size smaller than previously possible. This potentially allows a higher percentage of drug to be delivered into the lung in a shorter period of time. We believe this may reduce the amount of drug deposited in the back of the mouth and throat where it may result in local and systemic side effects.

Unit Dose Budesonide (UDB) Clinical Development Program

UDB is our proprietary nebulized version of budesonide for the potential treatment of asthma in children from 12 months to eight years of age. In a Phase 2 clinical trial, UDB was effective in improving asthma symptoms and was well tolerated when compared to placebo. Nebulization time was three to five minutes. In February 2009, we announced top-line results from our first Phase 3 trial of UDB, indicating that the trial did not meet its co-primary endpoints when compared to placebo. On July 8, 2009, our partner AstraZeneca AB terminated our worldwide collaboration agreement related to the UDB product candidate. Subsequently, we suspended development of UDB. We are considering options for our pediatric asthma program moving forward, by leveraging our experience with budesonide and our expertise in particle technology, including the development of a next generation therapy with budesonide.

Phase 3 Clinical Trial Results. In February 2009, we announced top-line results from our first Phase 3 trial of UDB, indicating that the trial did not meet its co-primary endpoints, asthma control as assessed by changes from baseline in nighttime and daytime composite symptom scores, in the two doses evaluated, when compared to placebo.

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In this randomized, double-blind, placebo-controlled trial, 360 steroid naïve children with asthma, 12-months to eight years of age, were randomized to receive 0.25 mg UDB, 0.135 mg UDB or placebo twice a day over a 12-week period. The co-primary endpoints evaluated asthma control as assessed by changes from baseline as compared to placebo in nighttime composite symptom scores, and daytime composite symptom scores, both comprised of cough, wheeze and shortness of breath. Based on our review of these data, both the placebo and active groups experienced improvements in asthma symptoms, but the differences between placebo and active were not statistically significant. We observed a higher than expected response in the placebo groups, starting as early as one week after randomization and continuing throughout the 12-week treatment period, suggesting that patients had milder asthma symptoms than anticipated, which made it difficult to show statistically significant separation between active and placebo groups. Median nebulization times were less than four minutes for both doses in the study. Review of the data has not identified any serious adverse events attributed to the study drug.

Phase 2 Clinical Trial Results. In February 2007, we announced positive results from a Phase 2 clinical trial of UDB as a potential treatment for asthma in children. The clinical trial included 205 asthmatic children aged one to 18 years old across multiple sites in the United States. The objective of the clinical trial was to evaluate the efficacy, tolerability and pharmacokinetics of UDB. The clinical trial compared two different doses of UDB, 0.135 mg and 0.25 mg, administered twice a day, in a randomized, double-blind, placebo-controlled trial. The co-primary endpoints of the clinical trial were the change from baseline in nighttime composite symptom score, which is a composite of the three symptoms of coughing, wheezing and shortness of breath, and the change from baseline in daytime composite symptom score in the same three symptoms. Secondary endpoints included changes from baseline in morning and evening peak expiratory flow, a measure of lung function. In addition, we evaluated trends in Forced Expiratory Volume in one second, or FEV_1, which indirectly measures airway narrowing.

This Phase 2 clinical trial demonstrated that after six weeks of dosing, UDB produced a statistically significant reduction in nighttime and daytime composite symptom scores versus placebo for the 0.135 mg dose of UDB ($p = 0.002$ for the nighttime score and $p = 0.003$ for the daytime score). Positive trends in FEV_1 were seen in those patients old enough to take this test. The higher 0.25 mg twice a day dose was not significantly better than placebo in the co-primary endpoints of nighttime and daytime composite symptom score. However, we observed consistent trends with respect to secondary endpoints and similar magnitude of FEV_1 improvements in both doses compared to placebo, which we believe is sufficient to support future clinical evaluation of the 0.25 mg dose.

The clinical trial showed both doses of UDB to be well tolerated, with no serious adverse events reported. There were no incidences of oral thrush. Also, there was no reduction in cortisol levels as compared to placebo over the duration of the clinical trial. Suppression of cortisol, a natural steroid hormone produced by the body, correlates with the occurrence of systemic side effects from the administration of high dose ICSs. Therefore, cortisol levels are often measured as an indication of systemic side effects from the administration of ICSs. Patients experienced average nebulization times of three to five minutes, which steadily decreased over the course of the clinical trial period.

MAP0005 Combination Particle Technology

We believe MAP0005 serves as a proof of concept for the robust, specific delivery of two therapeutic agents that could benefit from targeted receptor delivery in a fixed ratio within a single particle. We intend to opportunistically evaluate the application of this technology to additional product candidates because we believe our proprietary technologies in this area have potential broad applicability for a number of small molecule combination product candidates in diverse indications via inhalation and other routes of delivery. MAP0005, our proprietary combination of an inhaled corticosteroid and a long-acting beta-agonist, or LABA, for the potential treatment of asthma and chronic obstructive pulmonary disease, or COPD, utilizes our proprietary particle formulation technologies to administer the optimal ratio of multiple drugs in a reproducible and consistent

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manner. We combine two or more drugs together into a single micron sized particle at a pre-defined consistent and reproducible ratio, which may improve the delivery profile and stability of the resultant combination therapy. In April 2008, we announced positive results from a Phase 2a clinical trial evaluating MAP0005 for the potential treatment of asthma and COPD. We believe this approach, as compared to current ICS/LABA combinations, may allow the optimal ratio of each drug to the lung to reach the relevant receptors at the cellular level in the lung in a more reproducible and consistent manner, reducing the amount of drug delivered systemically and potentially improving the side effect profile, while improving therapeutic efficacy.

MAP0001 Stable Protein Particle Technology

We believe MAP0001 serves as proof of concept for the ability to formulate and stabilize biologically-active proteins and peptides and deliver them to the lung. We design and incorporate our protein formulations without the need for excipients or other additives, to be stored for months at room temperature and to provide multiple doses of medicine delivered accurately without the need for invasive needle injections. We intend to opportunistically evaluate the application of this technology to additional product candidates. We are demonstrating this capability with MAP0001, our proprietary formulation of insulin for the potential treatment of Type 1 and Type 2 diabetes via pulmonary delivery using our proprietary Tempo inhaler. In a Phase 1a clinical study conducted in Australia, MAP0001 was biologically active and achieved maximum therapeutic blood levels as quickly as Novorapid subcutaneous injection, a widely used injectable insulin.

We have not filed an IND with the FDA for MAP0005 or MAP0001 because our clinical trials were not conducted in the United States.

While we do not plan to make further significant direct investment in MAP0005 and MAP0001, we plan to evaluate other potential product candidates which may utilize these technologies, as well as partnership opportunities for further development and commercialization of these two product candidates.

Our Technology

Our aerosol delivery and pharmacological profiling technology combines our knowledge of aerosol science and medicine, and enables us to create inhaled drug products with potentially enhanced pharmacological profiles relative to the parent drugs, thereby improving their efficacy and safety. Starting with the bulk drug substance, we develop particles with the physical and chemical characteristics that are well suited for the aerosol delivery of the product candidate. The particle engineering allows more of our drug to reach the areas of the respiratory tract to treat disease and reduces the amount of drug that is deposited in the back of the throat where it can cause local and systemic side effects. We then formulate the drug particles into a delivery medium and package them into the aerosol delivery system that is best suited for the formulation and dosing regimen in order to maximize patient compliance. Our expertise in aerosol formulation science and pulmonary medicine allows us to select excipients, if any, already in wide use and regarded as safe, that result in favorable safety characteristics and allow flexibility in delivery format. The resulting drug products can be as consistent and efficient as alternative, often more invasive dosing formats, such as injection, but with the advantages of fast onset, high degree of intake at the target organs, and lower or controlled systemic exposure. The convenience, consistency and efficiency of inhaled administration in combination with the characteristics of our product candidates can offer meaningful therapeutic benefits when compared to existing drugs, increasing the probability of the successful adoption of our product candidates.

We apply our proprietary technologies to optimize drugs for two general types of therapeutic applications:

Delivery of drugs to treat respiratory diseases locally. Diseases such as asthma, COPD and some respiratory tract infections have been treated by pulmonary drug delivery for many years in order to target therapeutic effect to the lung and reduce systemic drug exposure and related side effects. Our technology is designed to improve the therapeutic efficacy and safety of known drugs for these

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applications, by efficiently delivering customized drug particles to those areas in the lung where drug is required and minimizing the drug exposure to other areas of the respiratory tract and body. In addition, our technologies have the potential to broaden the types of respiratory illnesses that can effectively be targeted and treated safely via pulmonary delivery.

Pulmonary delivery as a non-invasive method of quickly and safely administering systemic drugs. Administration of drugs via the respiratory tract is a non-invasive method of delivering drugs efficiently to the systemic circulation, with rapid onset of action, bypassing the gastrointestinal tract where many drugs are extensively metabolized after oral administration, and with rapid onset of action. The drug, or combination of drugs, can reach the intended site of action as quickly as intravenously administered drugs and more quickly than oral, dermal, sublingual or even alternative injection routes, such as subcutaneous or intramuscular. We can apply our technology to small or large molecules, including peptides and proteins.

Aerosol Delivery and Pharmacological Profiling Technology

Our proprietary technologies include particle creation and formulation technologies, which can be applied to small or large molecules, including peptides and proteins. Our technologies also include the development and manufacturing of aerosol delivery devices, including our current Tempo inhaler. Tempo is a proprietary, next generation pressurized metered dose inhaler, or MDI, that dispenses drug automatically when the patient inhales and has high consistency and efficiency compared to other inhalers. Our technologies are covered by over 25 issued U.S. patents and over 30 U.S. patent applications that we own or have licensed, as well as their foreign counterparts.

Particle Creation and Formulation

We control the characteristics of our drug particles by using technology and expertise in aerosol physics, particle science and formulation, and in safety toxicology and pharmacology. We can consistently generate drug-containing aerosols with the optimal particle or droplet sizes for the therapeutic indication. Particles that are too large tend to be deposited in the throat, while medium sized particles are more efficiently delivered to the large bronchial tubes and small particles are more efficiently delivered to the alveoli, the small sacks that make up most of the absorptive surface area of the lung. We can formulate product candidates in propellants without additional excipients, or with small amounts of excipients previously shown to be safe. We can also combine drugs by producing small, inhalable particles composed of one drug which is reproducibly intermingled or coated with multiple drugs in fixed ratios.

One of our key technologies is the generation of particles by supercritical fluid, or SCF, precipitation. SCF gives us the ability to create very small particles ranging from 100 nanometers to 10 microns in diameter with highly precise particle size distributions. The particles have uniform surfaces with few discontinuities or irregularities that provide enhanced aerosol performance. They are also stable for long storage periods without refrigeration, and require minimal or no excipients that can increase the potential for local toxicity or inflammatory response.

In addition to particle generation, we have extensive expertise in formulating aerosol drugs, especially for nebulized and MDI delivery formats. A key feature of this expertise is our know-how in formulating aerosolized drugs with appropriate excipients. We have expertise in formulation screening, assay development, aerosol performance testing and clinical performance simulation, long-term stability testing, large volume non-clinical testing and generation and release of pre-clinical and clinical supplies through to human clinical proof of concept.

We believe that the combination of these various particle creation and formulation technologies is a key component of our competitive advantage.

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Tempo Inhaler Platform

We designed our proprietary Tempo inhaler to enable accurate and reproducible pulmonary delivery of the drug particles we develop. Our Tempo inhaler is an innovative next generation MDI. The Tempo inhaler incorporates the size, ease of use and convenience advantages associated with standard MDIs, and is designed to overcome their greatest limitations: inconsistent dosing, drug delivery inefficiency and the need for patients to synchronize a breath with manual triggering of the device, which is particularly difficult for certain patient populations such as children and elderly patients. Even the more recently introduced breath-actuated MDIs exhibit the inconsistent dosing and drug delivery inefficiency of older MDIs.

The Tempo inhaler is designed to offer a number of key competitive advantages compared to standard MDIs. These advantages include:

Automatic, optimal release of therapy: Our triggering technology is tuned for each particular drug so that drug release is synchronized to the optimal point in the breathing cycle to allow the released drug to reach the targeted area of the respiratory tract. For example, data from a clinical trial showed that the Tempo inhaler deposited 75% less of a corticosteroid in the mouth and throat and delivered three times as much drug to the lungs as a conventional MDI.

Plume speed control: Conventional MDIs spray plumes of drug at speeds of up to 50 miles per hour, causing much of the drug to hit the back of the throat. By contrast, our Tempo inhaler controls and slows down the drug plume to match the speed of the patient s inhaled breath, so more of the drug is entrained in the inhaled air and carried into the lungs.

Dose consistency: Our clinical trials indicate that the Tempo inhaler s dose-to-dose consistency is comparable to oral dosing. The Tempo inhaler also includes a dose counter to display how many doses have been administered so patients can track their medication use and remaining supply. The dose counter can lock out the device after a maximum number of doses have been delivered to prevent overdosing.

Convenient, multiple dose use: The Tempo inhaler does not use electronics or batteries, can conveniently contain multiple doses and is relatively efficient to manufacture. It can include up to a month s supply depending on the drug, in a small, handheld package approximately the same size as a conventional MDI and it may be used with small molecule drugs and biologics.

The FDA issued draft guidelines in 1998 covering the MDI performance that the FDA would like MDI manufacturers to achieve. However, the FDA has not implemented the new guidelines to date, in part because conventional MDIs may not be capable of meeting them. We believe that our Tempo inhaler may meet the FDA s draft guidelines should the FDA elect to implement the guidelines at a future date.

We have conducted clinical trials with three clinical product candidates which utilize our Tempo inhaler: LEVADEX for the potential treatment of migraine, MAP0005 for the potential treatment of asthma and COPD and MAP0001 for the potential treatment of diabetes.

Our Strategy

Key elements of our strategy include:

Obtain regulatory approval for our most advanced product candidate LEVADEX: LEVADEX is being evaluated in a Phase 3 clinical program. We believe the risk of clinical trial failure may be lower than traditional new chemical entities because we are evaluating drugs that have been previously reviewed and approved by the FDA and have a known safety and efficacy profile.

Advance and expand our product pipeline in our target commercial areas, leveraging our extensive expertise in pulmonary delivery and respiratory science and medicine in a lower risk manner: We intend to focus our pipeline development initially on products with established safety and efficacy

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records, but whose market potential has been limited by safety, relative efficacy and patient compliance. We believe that we can overcome these limitations by leveraging our technologies. These technologies underpin our competitive advantage in developing multiple, high-value products with clearly defined patient benefits.

Build a focused sales force to commercialize LEVADEX: Our goal is to build a focused sales force in the United States to market and sell our products, once approved, to neurologists and headache specialists. We plan to develop or in-license additional product candidates for this sales force and any other sales forces we may develop.

Expand the market opportunity for our most advanced product candidates: In order to expand the commercial opportunity for LEVADEX, we may establish partnerships with pharmaceutical companies to market and sell to primary care physicians. Outside the United States, we may establish commercial partnerships for all of our product candidates in order to accelerate development and regulatory approvals in those countries and further broaden their commercial potential.

Collaborations and License Agreements

AstraZeneca

In December 2008, we entered into an agreement with AstraZeneca, or the AstraZeneca Agreement, which became effective in February 2009. Pursuant to the terms of the agreement, we licensed to AstraZeneca global rights to develop and commercialize our proprietary nebulized formulation of UDB, our next generation UDB therapy and certain combination nebulization therapies for the potential treatment of asthma in children.

In February 2009, under the terms of this agreement, AstraZeneca paid us a nonrefundable upfront cash payment of $40.0 million. On February 23, 2009, we announced top-line results of our initial Phase 3 clinical trial of UDB for the potential treatment of children with asthma. We announced that the clinical trial did not meet its co-primary endpoints, asthma control as assessed by changes from baseline in nighttime and daytime composite symptom scores, in either of the doses evaluated when compared with placebo.

On July 8, 2009, we received notice from AstraZeneca of the termination of the AstraZeneca Agreement, effective immediately. AstraZeneca elected to terminate the AstraZeneca Agreement pursuant to Section 19.3.1(b) of the AstraZeneca Agreement, which provides that AstraZeneca could terminate the AstraZeneca Agreement in the event that the primary endpoints of the initial Phase 3 clinical trial of UDB were not met. Effective on the date of termination, all rights licensed to AstraZeneca in the agreement reverted back to us. We also announced our plan to suspend development of our UDB product candidate. We were jointly developing UDB with AstraZeneca, and were responsible for executing the development plan.

Elan Pharma International

In April 2004 we entered into a license agreement with Elan Pharma International Limited, or Elan, which was superseded in February 2005 by an agreement that clarified the rights previously granted in 2004, and amended in June 2007. We also entered into a services agreement with Elan Drug Delivery International in February 2005.

Under the terms of this license agreement, Elan granted to us a worldwide, exclusive, sublicensable license under Elan s intellectual property rights to use, market, distribute, sell, have sold, offer for sale, import and export aqueous formulations of budesonide (alone or with certain other active ingredients) for pulmonary delivery using certain devices for therapeutic use in humans.

Elan also granted to us, subject to the execution of a manufacturing process transfer agreement, or manufacturing agreement, a non-exclusive sublicensable license in the same field as the exclusive license under its intellectual property rights to make and have made a bulk intermediate form of budesonide in certain countries including Canada, the United States, Ireland, certain countries in Europe, Japan, Australia and New Zealand.

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Elan granted to us a worldwide non-exclusive, sublicensable license to all improvements to its intellectual property rights arising as a direct result of the performance under the license agreement, the services agreement, and/or the manufacturing agreement.

In connection with the execution of the AstraZeneca Agreement, we amended the Elan agreements, so that we and AstraZeneca would have certain rights under the Elan agreements during the term of the AstraZeneca Agreement. Effective on the date of the termination from AstraZeneca, all rights licensed to AstraZeneca in the agreement reverted back to us.

Under the license agreement, we are required to make payments to Elan based upon achievement of certain development and sales milestones. As of December 31, 2009, when and if certain milestones are met we may be obligated to pay Elan up to $16.5 million in total future development and sale milestone payments with respect to our UDB product candidate. In addition, we are also required to make payments to Elan with respect to other product candidates we may develop pursuant to the license agreement. We are also required to pay royalties based on net sales of the product for an initial royalty term, calculated on a country-by-country basis, equal to either the expiration of Elan s patents covering the product in such country, or 15 years after commercial launch in such country, if Elan does not have patents covering the product in such country. After the initial royalty term, we continue to pay royalties on product sales to Elan at reduced rates.

Either party may terminate the agreement upon a material, uncured default of the other party. We may terminate the agreement, with or without cause, at any time upon 90 days written notice.

Nektar Therapeutics

We entered into a license agreement with Nektar Therapeutics UK Limited, or Nektar, in June 2004, and amended the agreement in August 2006 and October 2007. Under the agreement, Nektar granted us a worldwide, exclusive license, with a right to sublicense, under Nektar patents and know-how to develop and commercialize any formulation of a form of dihydroergotamine for administration by inhalation using a device. The Nektar patents licensed to us include two types of patent claims: compound-limited claims and compound-inclusive claims. Compound-limited claims are Nektar patent claims that claim a form of dihydroergotamine, or formulations or methods of manufacture or methods of use of dihydroergotamine, and our license to these claims is fully-paid up and royalty free and will survive expiration or any termination of the agreement. Compound-inclusive claims are Nektar patent claims that are not compound-limited claims and our license to these claims is royalty-bearing.

Our obligation to pay royalties to Nektar is based on net sales of products, and will continue, on a country-by-country basis, until the longer of expiration of Nektar patents covering the product, ten years after the first commercial sale of the product, or the date that Nektar s know-how becomes known to the general public. In addition, we are required to make future payments based upon achievement of certain product development milestones. As of December 31, 2009, when and if certain milestones are achieved we may be obligated to pay Nektar up to $5.0 million in total future development milestone payments with respect to our LEVADEX product candidate.

Under the agreement, we granted Nektar a worldwide, nonexclusive, royalty-free license under our patents and know-how solely to the extent useful or necessary for Nektar to fulfill its obligations under the agreement.

Either party may terminate the agreement upon a material, uncured default of the other party. We may terminate the agreement, with or without cause, at any time upon six months written notice.

Exemplar Pharmaceuticals

In April 2006 we entered into a manufacturing and supply agreement with Exemplar Pharmaceuticals, LLC, or Exemplar, formerly known as Xemplar Pharmaceuticals, LLC, for the manufacture and supply by Exemplar to us of our clinical and commercial requirements of pressurized metered dose aerosol canisters containing placebo or active ingredient that are housed within a fully-assembled Tempo inhaler and packaged for clinical and commercial use.

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Exemplar agreed to convert its manufacturing facility into a Good Manufacturing Practices, or GMP, contract manufacturing facility suitable for the commercial production of the product prior to or when Exemplar obtains the approvals necessary to manufacture these products in compliance with the manufacturing agreement.

We have agreed that, from the date the first NDA is submitted for a product and for a period of five years thereafter we will purchase the fully-assembled Tempo inhalers only from Exemplar, and Exemplar will manufacture and supply from its manufacturing facility all such devices as we require to support development and commercialization. If Exemplar fails to supply on time under certain circumstances, we have the right to immediately terminate the manufacturing agreement by written notice and to manufacture the product ourselves or purchase it from a third party.

Either party may terminate the agreement upon a material, uncured breach or default by the other party. We may terminate the agreement upon 60 days written notice upon our reasonable determination that Exemplar does not have the capability to manufacture the product in accordance with the warranty or in sufficient quantities.

Intellectual Property

We protect our technology through the use of patents, trade secrets and proprietary know-how. We own or in-license seven issued U.S. patents, and 13 U.S. patent applications, as well as their foreign counterparts, which relate to our most advanced product candidate LEVADEX. The patents and patent applications that may issue that we own or in-license, which we rely on for LEVADEX, expire between 2017 and 2030. Our patent and patent applications relating to LEVADEX include claims covering:

- various formulations of the LEVADEX active ingredient;
- the processing of the LEVADEX active ingredient;
- stabilization of the formulation;
- pharmacokinetics of the active ingredient delivered by the inhalation system; and
- the treatment of migraine via delivery of the formulation to the lung.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our product candidates, and the methods used to manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to protect our product candidates from unauthorized making, using, selling, offering to sell or importation by third parties is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We have rights to several third-party proprietary processing and manufacturing technologies related to our product candidates. See Collaborations and License Agreements. We rely on such third parties to protect the intellectual property we license, and we do not and have not had any control over the filing or prosecution of patent applications. We cannot be certain that such prosecution efforts have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents. Our enforcement of these licensed patents or defense of any claims asserting the invalidity of these patents would also be subject to the cooperation of the third parties.

Manufacturing

All of our manufacturing processes, which comply with current good manufacturing practices, or cGMP, are outsourced to third parties with oversight by our internal managers. We have limited cGMP manufacturing capacity in-house. We rely on third-party manufacturers to produce sufficient quantities of drug product for use in clinical trials. We intend to continue this practice for any future clinical trials and large-scale commercialization of LEVADEX and for any other potential products for which we retain significant development and commercialization rights.

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The bulk drug substance of LEVADEX has been manufactured by a contract manufacturing organization, or CMO, located in Europe. Our CMO has extensive experience manufacturing bulk drug under cGMP and has the capacity to manufacture at commercial scale. We are exclusive licensees of the manufacturing process for production of LEVADEX final drug substance. Under our worldwide license from Nektar, we have enabled another CMO to manufacture clinical and commercial supply of the final drug substance to be used in the development and commercialization of LEVADEX.

The Tempo inhaler is manufactured by third-party CMOs. The plastic inhaler component manufacture and assembly, valve manufacture and canister fill are each performed by specific third-party CMOs. Each has extensive experience with medical-grade clinical and commercial scale product manufacture under cGMP.

Competition

The pharmaceutical industry is highly competitive, with a number of established, large pharmaceutical companies, as well as many smaller companies. Many of these companies have greater financial resources, marketing capabilities and experience in obtaining regulatory approvals for product candidates. There are many pharmaceutical companies, biotechnology companies, public and private universities, government agencies and research organizations actively engaged in research and development of products which may target the same markets as our product candidates. We expect any future products we develop to compete on the basis of, among other things, product efficacy and safety, time to market, price, extent of adverse side effects experienced and convenience of administration and drug delivery. One or more of our competitors may develop products based upon the principles underlying our proprietary technologies earlier than us, obtain approvals for such products from the FDA more rapidly than us or develop alternative products or therapies that are safer, more effective and/ or more cost effective than any future products developed by us. We also expect to face competition in our efforts to identify appropriate collaborators or partners to help commercialize our product candidates in our target commercial areas.

If approved for the acute treatment of migraine, we anticipate that LEVADEX would compete against other marketed migraine therapies. In 2008, according to market data, approximately 29 million prescriptions were written for the treatment of migraine in the United States. Approximately 12 million of those prescriptions were written for acute migraine specific drugs. The majority of acute migraine specific drug prescriptions written were in the triptan class. In 2009, the triptan market in the United States totaled approximately $2.1 billion in revenues. The largest selling triptan is sumatriptan with 2009 sales of approximately $800 million in the United States including approximately $600 million from generics and $200 million from branded Imitrex from GlaxoSmithKline. There are six other branded triptan therapies being sold by pharmaceutical companies. Alternative formulations of triptans are available which may have faster onset of action than solid oral dosage forms. Alternative formulations of DHE include Migranal, which is nasally delivered. In April 2008, GlaxoSmithKline s Treximet, a combination oral formulation of sumatriptan and naproxen sodium, was approved by the FDA for the acute treatment of migraine. In July 2009, Zogenix, Inc s Sumavel DosePro needle-free sumatriptan was approved by the FDA for the treatment of acute migraine and cluster headache. In addition to marketed migraine therapies, there are several product candidates under development that could potentially be used to treat migraine and compete with LEVADEX, including products under development by large pharmaceutical companies such as Merck & Co., Inc. and other smaller companies. Merck s MK-097, a calcitonin gene-related peptide antagonist, is in Phase 3 development.

In addition, we may face competition from generic sumatriptan, the active ingredient in Imitrex. Although generic sumatriptan could not be substituted for LEVADEX, a generic version of sumatriptan may be more quickly adopted by health insurers and consumers than LEVADEX, as financial pressure to use generic products and uncertainty of reimbursement for single source alternatives, such as LEVADEX, may encourage the use of a generic product over LEVADEX. However, we believe that LEVADEX, if approved, will have features that may differentiate it from generic sumatriptan, and may be useful in patient populations that often do not respond to triptans.

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Government Regulation

Federal Food, Drug and Cosmetic Act

Prescription drug products are subject to extensive pre- and post-market regulation by the FDA, including regulations that govern the testing, manufacturing, safety, efficacy, labeling, storage, record keeping, advertising, and promotion of such products under the Federal Food, Drug and Cosmetic Act, or FFDCA, and its implementing regulations, and by comparable agencies and laws in foreign countries. Failure to comply with applicable FDA or other requirements may result in civil or criminal penalties, recall or seizure of products, partial or total suspension of production or withdrawal of the product from the market. FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. All applications for FDA approval must contain, among other things, information relating to safety and efficacy, pharmaceutical formulation, stability, manufacturing, processing, packaging, labeling and quality control.

New Drug Applications

A new drug approval by the FDA is generally required before a drug may be marketed in the United States. This process generally involves:

- completion of pre-clinical laboratory and animal testing in compliance with the FDA s Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND application for human clinical testing which must become effective before human clinical trials may begin in the United States;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug product for each intended use;
- satisfactory completion of an FDA pre-approval inspection of the facility or facilities at which the product is manufactured to assess compliance with the FDA s cGMP regulations; and
- submission to and approval by the FDA of an NDA application.

The pre-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Pre-clinical tests include laboratory evaluation of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animals. The results of pre-clinical tests, together with manufacturing information and analytical data, are submitted as part of an IND application to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30 day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development. Further, an independent institutional review board, or IRB, covering each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center and it must monitor the clinical trial until completed. The FDA, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. As a separate amendment to an IND, a sponsor may submit a request for a SPA from the FDA. Under the SPA procedure, a sponsor may seek the FDA s agreement on the design and size of a clinical trial intended to form the primary basis of an efficacy claim. If the FDA agrees in writing, its agreement may not be changed after the clinical trial begins, except in limited circumstances, such as when a substantial scientific issue essential to determining the safety and effectiveness of a product candidate is identified after a Phase 3 clinical trial is commenced. If the outcome of the clinical trial is successful, the sponsor will ordinarily be able to rely on it as the primary basis for approval with respect to effectiveness. Clinical testing also must satisfy extensive Good Clinical Practice, or GCP, regulations, including regulations for informed consent.

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For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following three sequential phases, which may overlap:

Phase 1: Clinical trials are initially conducted in a limited population to test the product candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients, such as cancer patients.

Phase 2: Clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more extensive Phase 3 clinical trials. In some cases, a sponsor may decide to run what is referred to as a Phase 2b evaluation, which is a second, confirmatory Phase 2 clinical trial that could, if positive and accepted by the FDA, serve as a pivotal trial in the approval of a product candidate.

Phase 3: These are commonly referred to as pivotal clinical trials. When Phase 2 evaluations demonstrate that a dose range of the product is effective and has an acceptable safety profile, Phase 3 clinical trials are undertaken in large patient populations to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically-dispersed clinical trial sites.

Phase 4: These are clinical trials conducted after a drug has been approved. In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor s agreement to conduct additional clinical trials to further assess the drug s safety and effectiveness after NDA approval. Such post approval trials are typically referred to as Phase 4 clinical trials.

The results of product development, pre-clinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs must also contain extensive manufacturing information. Once the submission has been accepted for filing, by law the FDA has 180 days to review the application and respond to the applicant. Under the Prescription Drug User Fee Act, or PDUFA, the FDA agrees to specific goals for NDA review time through a two-tiered classification system, Standard Review and Priority Review. Standard Review is applied to a drug that offers at most only minor improvement over existing marketed therapies. Standard Review NDAs have a goal of being completed within a 10-month timeframe. A Priority Review designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A Priority Review means that the time it takes the FDA to review an NDA is reduced such that the goal for completing a Priority Review initial review cycle is six months. It is likely that our product candidates will be granted a Standard Review. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

The FDA may deny approval of an NDA if the applicable regulatory criteria are not satisfied, or it may require additional clinical data and/or an additional pivotal Phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and FDA may interpret data differently than we do. Once issued, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing, including Phase 4 clinical trials and surveillance programs, to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these postmarketing programs. Drugs may be marketed only for approved indications and in accordance with the provisions of the approved label. Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require us to develop additional data or conduct additional pre-clinical studies and clinical trials.

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Section 505(b)(2) New Drug Applications

As an alternate path to FDA approval for modifications to formulations of products previously approved by the FDA, an applicant may file an NDA under Section 505(b)(2) of the FFDCA. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, and permits the filing of an NDA where at least some of the information required for approval comes from clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The Hatch Waxman Act permits the applicant to rely upon the FDA s findings of safety and effectiveness based on certain pre-clinical or clinical trials conducted for an approved product. The FDA may also require companies to perform additional clinical trials or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that a Section 505(b)(2) NDA relies on clinical trials conducted for a previously approved drug product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book. Specifically, the applicant must certify for each listed patent that (1) the required patent information has not been filed; (2) the listed patent has expired; (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patent is invalid, unenforceable or will not be infringed by the new product. A certification that the new product will not infringe the already approved product s listed patent or that such patent is invalid is known as a Paragraph IV certification. If the applicant does not challenge the listed patents through a Paragraph IV certification, the Section 505(b)(2) NDA application will not be approved until all the listed patents claiming the referenced product have expired. The Section 505(b)(2) NDA application also will not be accepted or approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a New Chemical Entity, listed in the Orange Book for the referenced product, has expired.

If the 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the referenced NDA and patent holders once the 505(b)(2) NDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a legal challenge to the Paragraph IV certification. Under the FFDCA, the filing of a patent infringement lawsuit within 45 days of their receipt of a Paragraph IV certification automatically prevents the FDA from approving the Section 505(b)(2) NDA for 30 months, or until a court decides that the patent is invalid, unenforceable or not infringed, whichever is earlier. The court also has the ability to shorten or lengthen the 30 month stay if either party is found not to be reasonably cooperating in expediting the litigation. Thus, the Section 505(b)(2) applicant may invest a significant amount of time and expense in the development of its product only to be subject to significant delay and patent litigation before its product may be commercialized. Alternatively, if the listed patent holder does not file a patent infringement lawsuit within the required 45 day period, the applicant s NDA will not be subject to the 30 month stay.

DEA Regulation

Our research and development processes involve the controlled use of hazardous materials, including chemicals. Some of these hazardous materials are considered to be controlled substances and subject to regulation by the U.S. Drug Enforcement Agency, or the DEA. Controlled substances are those drugs that appear on one of five schedules promulgated and administered by the DEA under the Controlled Substances Act, or CSA. The CSA governs, among other things, the distribution, recordkeeping, handling, security and disposal of controlled substances. We must be registered by the DEA in order to engage in these activities, and are subject to periodic and ongoing inspections by the DEA and similar state drug enforcement authorities to assess ongoing compliance with the DEA s regulations. Any failure to comply with these regulations could lead to a variety of sanctions, including the revocation, or a denial of renewal, of the DEA registration, injunctions or civil or criminal penalties.

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International Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of any future products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

For example, under European Union regulatory systems, marketing authorizations may be submitted either under a centralized or mutual recognition procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

In addition to regulations in Europe and the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial distribution of any future products.

Third-Party Payor Coverage and Reimbursement

Although none of our product candidates has been commercialized for any indication, if they are approved for marketing, commercial success of our product candidates will depend, in part, upon the availability of coverage and reimbursement from third-party payors at the federal, state and private levels. Government payor programs, including Medicare and Medicaid, private health care insurance companies and managed care plans have attempted to control costs by limiting coverage and the amount of reimbursement for particular procedures or drug treatments. The United States Congress and state legislatures from time to time propose and adopt initiatives aimed at cost containment. Ongoing federal and state government initiatives directed at lowering the total cost of health care will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid payment systems. Examples of how limits on drug coverage and reimbursement in the United States may cause reduced payments for drugs in the future include:

changing Medicare reimbursement methodologies;

fluctuating decisions on which drugs to include in formularies;

revising drug rebate calculations under the Medicaid program; and

reforming drug importation laws.

Some third-party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse health care providers that use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and operate profitably.

Manufacturing Requirements

We and our third-party manufacturers must comply with applicable FDA regulations relating to FDA s cGMP regulations. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements to the satisfaction of the FDA pursuant to a pre-approval inspection before we can use them to

manufacture our products. We and our third-party manufacturers are also subject to periodic inspections of

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facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations. Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties. Adverse experiences with the product must be reported to the FDA and could result in the imposition of market restrictions through labeling changes or in product removal. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval.

Other Regulatory Requirements

With respect to post-market product advertising and promotion, the FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among other things, standards for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. The FDA has very broad enforcement authority under the FFDCA, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing entities to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA and state and federal civil and criminal investigations and prosecutions.

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA has broad regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products and withdraw approvals, any one or more of which could have a material adverse effect on us.

Employees

As of December 31, 2009, we employed 82 full-time employees. Of the full-time employees, 58 were engaged in product development and clinical activities, and 24 were engaged in sales, general and administrative activities. We plan to continue to expand our product development programs. To support this growth, we will need to expand managerial, operations, development, regulatory, sales, marketing, finance and other functions. None of our employees are represented by a labor union, and we consider our employee relations to be good.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. The public may read or copy any materials we file with the SEC at the SEC s Public Reference Room at 450 Fifth Street, NW, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov.

We incorporated in the state of Delaware, were originally formed as a limited liability company on July 3, 2003 and converted to a corporation on December 11, 2003. We completed our initial public offering in October 2007 and a follow-on public offering in August 2009. Our principal executive offices are located at 2400 Bayshore Parkway, Suite 200, Mountain View, California, 94043. Our telephone number is (650) 386-3100, and our web site address is *www.mappharma.com*. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports are available free of charge on our web site as soon as reasonably practicable after we file these reports with the SEC. Our Code of Ethics can also be found on our website.

Financial Information

See Item 6, *Selected Financial Data* and Item 7*, Management s Discussion and Analysis of Financial Condition and Results of Operations.*

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ITEM 1A. RISK FACTORS

Certain factors may have a material adverse effect on our business, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this report as well as our other public filings with the Securities and Exchange Commission.

Risks Relating to Our Financial Position and Need for Additional Capital

We have a history of net losses. Currently, we have no products approved for commercial sale, and to date we have not generated any product revenue. As a result, we expect to continue to incur substantial and increasing net losses for the foreseeable future, and we may never achieve or maintain profitability.

We are not profitable and do not expect to be profitable in the foreseeable future. We have incurred significant net losses and negative cash flow in each year since our inception, including net losses of approximately $40.1 million, $72.9 million and $9.0 million, for the years ended December 31, 2007, 2008 and 2009, respectively. As of December 31, 2009, we had a deficit accumulated during development stage of approximately $184.9 million. We have devoted most of our financial resources to research and development, including our pre-clinical development activities and clinical trials. We have not completed development of, or commercialized, any product candidate and have therefore not generated any product revenues. In that regard, we expect to have substantial expenses as we continue with our Phase 3 clinical program for LEVADEX, our most advanced product candidate, and conduct other clinical trials. In addition, if we are required by the U.S. Food and Drug Administration, or the FDA, to perform studies in addition to those we currently anticipate, our expenses will increase beyond expectations and the timing of any potential product approval may be delayed. We also expect an increase in our expenses associated with our manufacturing work and with preparing for commercialization. In addition, we expect to continue to incur costs to support operations as a public company. As a result, we may continue to incur substantial net losses and negative cash flow for the foreseeable future. These losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders equity and working capital.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of substantial expenses or when, or if, we will be able to achieve or maintain profitability. We have financed our operations primarily through the sale of equity securities, collaboration payments and debt financings. The size of our future net losses will depend, in part, on the rate of growth of our expenses and the rate of growth, if any, of our revenues. Revenues from potential strategic partnerships are uncertain because we may not enter into any additional strategic partnerships. On July 8, 2009, we received a notice of termination of our license agreement with AstraZeneca related to our Unit Dose Budesonide, or UDB, product candidate. Under the AstraZeneca Agreement, AstraZeneca had agreed to fund our remaining development activities for UDB and to reimburse us for costs we incur with respect to future UDB development activities conducted for the U.S. registration, subject to the terms and conditions of the license agreement. Following the termination of the license agreement, we suspended development of UDB. If we are unable to develop and commercialize our other product candidates or if sales revenue from any product candidate that receives marketing approval is insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability.

We have a limited operating history, and we expect a number of factors to cause our operating results to fluctuate on a quarterly and annual basis, which may make it difficult to predict our future performance.

Our operations to date have been primarily limited to organizing and staffing our company, developing our technology and undertaking pre-clinical studies and clinical trials of our product candidates. We have not yet obtained regulatory approvals for any of our product candidates. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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Specifically, our financial condition and operating results have varied significantly in the past and will continue to fluctuate from quarter-to-quarter and year-to-year in the future due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include the following factors, among others:

- our ability to obtain additional funding to develop our product candidates;
- the need to obtain regulatory approval of our most advanced product candidate, LEVADEX for the potential treatment of migraine;
- potential risks related to any collaborations we may enter into for our product candidates, including LEVADEX;
- delays in the commencement, enrollment and completion of clinical testing, as well as the analysis and reporting of results from such clinical testing;
- the success of clinical trials of our LEVADEX product candidate or future product candidates;
- any delays in regulatory review and approval of product candidates in development;
- the FDA s determination of the special protocol assessment, or SPA, we entered into for LEVADEX;
- our ability to rely on Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FFDCA, to seek FDA marketing approval of our product candidates;
- our ability to rely on Section 505(b)(2) of the FFDCA;
- market acceptance of our product candidates for which we obtain regulatory approval;
- our ability, and our partners ability, to establish an effective sales and marketing infrastructure;
- competition from existing products or new products that may emerge;
- the impact of competition, including generics, in the migraine market on our ability to commercialize LEVADEX;
- the ability of patients to obtain coverage of or sufficient reimbursement for our products outside of the United States;
- the ability to receive regulatory approval or commercialize our products;

potential side effects of our future products that could delay or prevent commercialization or cause an approved drug to be taken off the market;

regulatory difficulties relating to products that have already received regulatory approval;

guidelines and recommendations of therapies published by various organizations;

potential product liability claims;

potential liabilities associated with hazardous materials;

our ability to maintain adequate insurance policies;

our dependency on third-party manufacturers to supply or manufacture our products;

our ability to establish or maintain collaborations, licensing or other arrangements;

our ability, our partners abilities, and third parties abilities to protect and assert intellectual property rights;

costs related to and outcomes of potential intellectual property litigation;

compliance with obligations under intellectual property licenses with third parties;

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our ability to adequately support future growth; and

our ability to attract and retain key personnel to manage our business effectively.

Due to the various factors mentioned above, and others, the results of any prior quarterly or annual periods should not be relied upon as indications of our future operating performance.

We will need substantial additional funding and if we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs.

Developing biopharmaceutical products, including conducting pre-clinical studies and clinical trials and establishing manufacturing capabilities, is expensive. We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we focus on and proceed with our Phase 3 clinical program and conduct our other clinical trials of LEVADEX, our most advanced product candidate. In addition, our expenses could increase beyond expectations if the FDA requires that we perform additional studies to those that we currently anticipate, in which case the timing of any potential product approval may be delayed. We believe that our existing cash, cash equivalents and short-term investments will be sufficient to fund our projected operating requirements for at least 12 months. We will need substantial additional capital in the future in order to complete the development and commercialization of LEVADEX and to fund the development and commercialization of future product candidates. Until we can generate a sufficient amount of product revenue, if ever, we expect to finance future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. Such funding, if needed, may not be available on favorable terms, if at all. In the event we are unable to obtain additional capital, we may delay or reduce the scope of our current research and development programs and other expenses.

As widely reported, financial markets in the United States, Europe and Asia have been experiencing extreme disruption, including, among other things, extreme volatility in security prices, severely diminished liquidity and credit availability, rating downgrades of certain investments and declining valuations of others. Governments have taken unprecedented actions intended to address extreme market conditions that include severely restricted credit and declines in real estate values. Concern about the stability of the markets generally and the strength of counterparties specifically has led many lenders and institutional investors to reduce, and in some cases, cease to provide funding to borrowers. Continued turbulence in the U.S. and international markets and economies may limit our ability to access the capital markets to meet our funding requirements.

If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or development programs or our commercialization efforts. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience additional significant dilution, and debt financing, if available, may involve restrictive covenants. To the extent that we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or our product candidates or to grant licenses on terms that may not be favorable to us. We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this Risk Factors section. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements will depend on many factors, including, but not limited to:

the scope, rate of progress and cost of our clinical trials and other research and development activities;

the costs and timing of regulatory approval;

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

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the effect of competing technological and market developments;

the terms and timing of any collaboration, licensing or other arrangements that we may establish;.

the cost and timing of completion of clinical and commercial-scale manufacturing activities; and

the costs of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval.

Risks Relating to the Development, Regulatory Approval and Commercialization of Our Product Candidates

We are largely dependent on the success of one product candidate, and we cannot be certain that this product candidate will receive regulatory approval.

We have invested a significant portion of our efforts and financial resources in the development of UDB and LEVADEX. In February 2009, we announced top-line results from our first Phase 3 trial of UDB, indicating that the trial did not meet its co-primary endpoints in either dose evaluated when compared to placebo. In July 2009 we announced that we were suspending development of UDB, after our partner AstraZeneca terminated our license agreement. We are now largely dependent on the success of one product candidate, LEVADEX, for which we are conducting a Phase 3 clinical development program. Our ability to generate product revenue, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development, regulatory approval and successful commercialization of this product candidate. We may have inadequate financial or other resources to advance LEVADEX through the clinical trial process, depending on the requirements of the FDA. In May 2009, we announced top-line results from the efficacy portion of our first Phase 3 trial of LEVADEX, indicating that the trial met all its co-primary endpoints when LEVADEX was compared to placebo. A long-term safety extension of the study is ongoing. Although we had planned to initiate a second Phase 3 efficacy study in the first quarter of 2010, we have been informed by the FDA that a second pivotal efficacy study is not required for submission of our NDA. We expect to conduct additional clinical trials, including a pharmacokinetics trial in approximately 24 adult smokers comparing them to approximately 24 non-smokers and a pharmacodynamics trial evaluating pulmonary artery pressure in healthy volunteers using echocardiogram before submitting an application to the FDA for regulatory approval. We expect treatment in our remaining LEVADEX clinical trials to be completed in 2010. Our clinical development program for LEVADEX may not lead to regulatory approval from the FDA and similar foreign regulatory agencies if we fail to demonstrate that the product candidate is safe and effective in our planned clinical trials, and we may therefore fail to commercialize LEVADEX. Any failure to obtain regulatory approval of LEVADEX would have a material and adverse impact on our business.

With the suspension of development for our UDB product candidate, LEVADEX is our only current product candidate in late stage development. Our drug development efforts may not produce any other proprietary product candidates. We cannot be certain that we will be able to acquire or in-license other product candidates or develop a next generation budesonide therapy for the treatment of asthma in children, should we pursue these activities. Our failure to develop product candidates will limit our ability to generate additional revenue.

We currently have no approved drug products for sale and we cannot guarantee that we will ever have marketable drug products. The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, with regulations differing from country to country. We are not permitted to market our product candidates in the United States until we receive approval of a new drug application, or an NDA, from the FDA for each product candidate. We have not submitted an NDA or received marketing approval for any of our product candidates. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. Markets outside of the United States also have requirements for approval of drug candidates which we must comply with prior to marketing.

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We may enter into collaborations with third parties to develop and commercialize our product candidates, including LEVADEX. These collaborations may place the development of our product candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

We may enter into collaborations with third parties to develop and commercialize our product candidates, including LEVADEX. Our dependence on future partners for development and commercialization of our product candidates will subject us to a number of risks, including:

- we may not be able to control the amount and timing of resources that our partners may devote to the development or commercialization of product candidates or to their marketing and distribution;
- partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- disputes may arise between us and our partners that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management s attention and resources;
- partners may experience financial difficulties;
- partners may not properly maintain or defend our intellectual property rights, or may use our proprietary information, in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or proprietary information or expose us to potential litigation;
- business combinations or significant changes in a partner s business strategy may adversely affect a partner s willingness or ability to meet its obligations under any arrangement;
- a partner could independently move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; and
- the collaborations with our partners may be terminated or allowed to expire, which would delay the development and may increase the cost of developing our product candidates. increase the cost of developing our product candidates.

Delays in the commencement, enrollment and completion of clinical testing could result in increased costs to us and delay or limit our ability to obtain regulatory approval for our product candidates.

Delays in the commencement, enrollment and completion of clinical testing could significantly affect our product development costs. We do not know whether planned clinical trials for LEVADEX will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials requires us to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs for the same indication as our product candidates or may be required to withdraw from our clinical trial as a result of changing standards of care or may become ineligible to participate in clinical studies. The commencement, enrollment and completion of clinical trials can be delayed for a variety of other reasons, including delays related to:

reaching agreements on acceptable terms with prospective contract research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

obtaining regulatory approval to commence a clinical trial;

obtaining institutional review board, or IRB, approval to conduct a clinical trial at numerous prospective sites;

recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including meeting the enrollment criteria for our study and competition from other clinical trial programs for the same indication as our product candidates;

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retaining patients who have initiated a clinical trial but may be prone to withdraw due to the treatment protocol, lack of efficacy, personal issues or side effects from the therapy or who are lost to further follow-up;

maintaining and supplying clinical trial material on a timely basis;

complying with design protocols of any applicable SPAs; and

collecting, analyzing and reporting final data from the clinical trials.

In addition, a clinical trial may be suspended or terminated by us, the FDA or other regulatory authorities due to a number of factors, including:

failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;

inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;

unforeseen safety issues or any determination that a trial presents unacceptable health risks; and

lack of adequate funding to continue the clinical trial, including unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties.

If we are required to conduct additional clinical trials or other testing of our LEVADEX product candidate beyond those that we currently contemplate, we may be delayed in obtaining, or may not be able to obtain, marketing approval for this product candidate. We currently are conducting a Phase 3 clinical program for LEVADEX and will need to complete our long-term safety extension and conduct a pharmacokinetics trial and a pharmacodynamics trial in order to support our new drug application for LEVADEX. We may not be able to obtain approval for indications that are as broad as intended or we may obtain approval for indications different than those indications for which we seek approval. Furthermore we may not be able to obtain approval for any of our other product candidates.

Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. Amendments may require us to resubmit our clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in the completion of, or if we terminate, our clinical trials, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Even if we are able to ultimately commercialize our product candidates, other therapies for the same or similar indications may have been introduced to the market and established a competitive advantage.

Because the results of prior clinical trials are not necessarily predictive of future results, LEVADEX or any other product candidate advanced into clinical trials may not have favorable results in subsequent clinical trials or receive regulatory approval.

Success in pre-clinical studies and clinical trials does not ensure that subsequent clinical trials will generate adequate data to demonstrate the efficacy and safety of the investigational drug. A number of companies in the pharmaceutical industry, including those with greater resources and experience, have suffered significant setbacks in Phase 3 clinical trials, even after seeing promising results in prior clinical trials.

In May 2009, we announced top-line results from the efficacy portion of our first Phase 3 trial of LEVADEX, indicating that the trial met all four of its co-primary endpoints when LEVADEX was compared to placebo. A long-term safety extension of the study is ongoing. In order to obtain regulatory approval for

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LEVADEX, we need to complete the long-term safety extension and conduct a pharmacokinetics trial and a pharmacodynamics trial. The data collected from our clinical trials may not be adequate to support regulatory approval of LEVADEX or any of our other product candidates. Even if we obtain regulatory approval of a product candidate, the FDA may require continuing evaluation and study of our product through clinical trials as a condition of any approval. Despite the results reported in prior clinical trials for our product candidates, we do not know whether subsequent clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market our product candidates. For example, after receiving positive data from a previous Phase 2 trial, in February 2009, we announced top-line results from our first Phase 3 trial of UDB, indicating that the trial did not meet its co-primary endpoints in either dose evaluated when compared to placebo.

If clinical trials of our LEVADEX product candidate or future product candidates do not produce results necessary to support regulatory approval in the United States or elsewhere or show undesirable side effects, we will be unable to commercialize these products.

To receive regulatory approval for the commercial sale of LEVADEX or any other product candidates, we must conduct adequate and well-controlled clinical trials to demonstrate efficacy and safety in humans. Clinical testing is expensive, takes many years and has an uncertain outcome. Clinical failure can occur at any stage of the testing. Our clinical trials may produce negative or inconclusive results. In such cases, we may decide, or regulators may require us, to conduct additional clinical and/or non-clinical testing, or we may decide not to pursue further development of a product candidate, such as the case of our UDB product candidate, where top-line results of our initial Phase 3 clinical trial indicated that the trial failed to meet the primary endpoints. Subsequently we suspended development of UDB. In addition, the results of our clinical trials may show that our product candidates may cause undesirable side effects, which could interrupt, delay or halt clinical trials, resulting in our inability to obtain regulatory approval by the FDA and other regulatory authorities.

In light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Government Accounting Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials and regulatory approval. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

Our failure to adequately demonstrate the efficacy and safety of LEVADEX or any other product candidates would prevent regulatory approval and, ultimately, the commercialization of that product candidate.

All of our product candidates in development require regulatory review and approval prior to commercialization. Any delay in the regulatory review or approval of any of our product candidates in development will harm our business.

All of our product candidates in development require regulatory review and approval prior to commercialization. Any delays in the regulatory review or approval of our product candidates in development would delay market launch, increase our cash requirements and result in additional operating losses.

The process of obtaining FDA and other required regulatory approvals, including foreign approvals, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. Furthermore, this approval process is extremely complex, expensive and uncertain. We or our partners may not be able to maintain our proposed schedules for the submission of any NDA in the United States or any marketing approval application or other foreign applications for any of our products. If we or our partners submit

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any NDA, including any amended NDA or supplemental NDA, to the FDA seeking marketing approval for any of our product candidates, the FDA must decide whether to either accept or reject the submission for filing. We cannot be certain that any of these submissions will be accepted for filing and reviewed by the FDA, or that our marketing approval application submissions to any other regulatory authorities will be accepted for filing and review by those authorities. We cannot be certain that we or our partners will be able to respond to any regulatory requests during the review period in a timely manner without delaying potential regulatory action. We also cannot be certain that any of our product candidates will receive favorable recommendation from any FDA advisory committee or foreign regulatory bodies or be approved for marketing by the FDA or foreign regulatory authorities. In addition, delays in approvals or rejections of marketing applications may be based upon many factors, including regulatory requests for additional analyses, reports, data and/or studies, regulatory questions regarding data and results, changes in regulatory policy during the period of product development and/or the emergence of new information regarding our products or other products.

Data obtained from pre-clinical studies and clinical trials are subject to different interpretations, which could delay, limit or prevent regulatory review or approval of any of our products. In addition, as a routine part of the evaluation of any potential drug, clinical studies are generally conducted to assess the potential for drug-drug interactions that could impact potential product safety. At this point in time, we have not been requested to perform drug-drug interaction studies, but any such request may delay any potential product approval and will increase our expenses associated with our clinical programs. Furthermore, regulatory attitudes towards the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects.

In addition, the environment in which our regulatory submissions may be reviewed changes over time. For example, average review times at the FDA for marketing approval applications have fluctuated over the last ten years, and we cannot predict the review time for any of our submissions with any regulatory authorities. In addition, review times can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes.

While we have negotiated an SPA with the FDA for our first Phase 3 clinical trial of LEVADEX for the potential treatment of migraine, the SPA does not guarantee any particular outcome from regulatory review of the study or the product candidate.

The FDA s SPA process creates a written agreement between the sponsoring company and the FDA regarding clinical trial design and other clinical trial issues that can be used to support approval of a product candidate. The SPA is intended to provide assurance that if the agreed upon clinical trial protocols are followed and the trial endpoints are achieved, the data may serve as the primary basis for an efficacy claim in support of an NDA. However, the SPA agreement is not a guarantee of an approval of a product or any permissible claims about the product. In particular, the SPA is not binding on the FDA if public health concerns unrecognized at the time of the SPA agreement is entered into become evident, other new scientific concerns regarding product safety or efficacy arise or if the sponsor company fails to comply with the agreed upon trial protocols. In January 2008, we announced that we reached agreement with the FDA on a SPA for the first Phase 3 clinical trial of our LEVADEX product candidate for the potential treatment of migraine. In May 2009, we announced top-line results from the efficacy portion of our first Phase 3 trial of LEVADEX, indicating that the trial met all its co-primary endpoints when LEVADEX was compared to placebo. A long-term safety extension of the study is ongoing. We cannot assure you that the safety extension of the Phase 3 clinical trial will be successful. In addition, we do not know how the FDA will interpret the commitments under the SPA agreement, how it will interpret the data and results or whether it will approve our LEVADEX product candidate for the treatment of migraine. As a result, we cannot guarantee any particular outcome from regulatory review of the first LEVADEX Phase 3 trial.

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We may not be able to rely on Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, which could result in a longer development program and more costly trials than we anticipate.

We may not be able to seek FDA marketing approval of our product candidates under Section 505(b)(2) of the FFDCA. Section 505(b)(2), if applicable to us, would allow an NDA we file with the FDA to rely in part on data in the public domain or the FDA s prior conclusions regarding the safety and effectiveness of approved compounds, which could expedite the development program for our product candidates by potentially decreasing the overall scope of work we must do ourselves. If we are unable to rely on Section 505(b)(2), the development program for our product candidates would be longer than we expect, and we would also have to conduct more costly trials than we anticipate.

If any of our product candidates for which we or our partners receive regulatory approval do not achieve broad market acceptance, the revenues that we generate from their sales will be limited.

The commercial success of our product candidates for which we or our partners obtain marketing approval from the FDA or other regulatory authorities will depend upon the acceptance of these products among physicians, the medical community, patients, and coverage and reimbursement of them by third-party payors, including government payors. The degree of market acceptance of any of our approved products will depend on a number of factors, including:

a product s FDA-approved labeling as well as limitations or warnings contained in the labeling;

changes in the standard of care for the targeted indications for any of our product candidates, which could reduce the marketing impact of any claims that we could make following FDA approval;

limitations inherent in the approved indication for any of our product candidates compared to more commonly understood or addressed medical conditions;

lower demonstrated efficacy and a less favorable safety or tolerability profile compared to other products;

device-related difficulties associated with our Tempo inhaler;